COVERAGE:

The following Tumor Necrosis Factor (TNF) Alpha inhibitors are considered medically necessary for the indications listed:

**Infliximab (Remicade)**

- Moderate to severe active Crohn’s disease for:
  - reduction of the signs and symptoms, and
  - maintenance of clinical remission

in patients who have an inadequate response to conventional therapy.

- Patients with fistulizing Crohn’s disease for the reduction in the number of draining enterocutaneous fistula(s).

- In combination with methotrexate, for use in the reduction of signs and symptoms, inhibiting the progression of structural damage, and improving physical function of patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to methotrexate alone.

  **Exception:** Infliximab (Remicade) used alone (for the reduction of signs and symptoms of RA) is allowed as an “off-label” use for those patients that cannot tolerate Methotrexate.

- Patients with spondlyarthropathy.

All other “off-label” uses of Infliximab (Remicade) are considered experimental or investigational, including, but not limited to, treatment of ulcerative colitis, arthritides other than RA (ie. psoriatic arthritis), and the dermatologic manifestations of psoriasis.

**Etanercept (Enbrel)**

For reduction in signs and symptoms and inhibiting the progression of structural damage in patients with moderate to severe active RA. Enbrel can be used in combination with methotrexate in patients who have had an inadequate response to methotrexate alone.

Enbrel is indicated for reducing signs and symptoms of moderate to severe active polyarticular-course juvenile RA in patients who have had an inadequate response to one or more disease-modifying antirheumatic drugs (DMARD’s).
Enbrel is indicated for reduction in signs and symptoms of active arthritis in patients with psoriatic arthritis. Enbrel can be used in combination with methotrexate in patients who have had an inadequate response to methotrexate alone.

Adalimumab (Humira)

Humira is indicated for reducing signs and symptoms and inhibiting the progression of structural damage in adult patients with moderately to severely active RA who have had an inadequate response to one or more DMARD’s. Humira can be used alone or in combination with methotrexate or other DMARD’s.

Infliximab (Remicade)

Infliximab (Remicade) is a murine-human chimeric monoclonal antibody, which binds to and neutralizes the effects of TNF. The binding of Remicade to TNF has been shown to be highly specific and dose dependent. TNF has been found in the joints of RA patients and in stools of patients with Crohn’s disease and correlates with elevated disease activity.

Infliximab (Remicade) is supplied as a sterile lyophilized powder for intravenous infusion.

Elevated levels of TNF have also been implicated in many inflammatory diseases and there has been interest in expanding the use of Infliximab (Remicade) for the following “off-label” indications:

- treatment of ulcerative colitis
- inflammatory arthritides such as ankylosing spondylitis and psoriatic arthritis,
- treatment of psoriatic skin lesions.

Etanercept (Enbrel)

Enbrel is a genetically engineered protein and represents a class of drugs for the treatment and management of RA. Enbrel binds to TNF, a naturally occurring protein in the body, and inhibits its action. TNF, which promotes inflammation in the body, is found at elevated levels in the fluid surrounding the affected joints of RA patients.

Although many patients with RA respond well to currently available
treatments, many are also disabled and suffer severe pain from the disease. It is estimated that RA, an autoimmune disease, affects more than two million Americans. As many as one third to one half of these people are estimated to have moderate to severe RA.

**Humira (adalimumab)**

Humira is a human-derived antibody that binds to human TNF alpha. TNF is naturally produced by the body and is involved with normal inflammatory and immune responses. By working against the inflammatory process, Humira, like other TNF blockers has been shown to be effective in controlling symptoms of the disease.

**RATIONALE:**

**Off-Label Uses of Infliximab**

As treatment of ulcerative colitis, arthritides other than RA, and the dermatologic manifestations of psoriasis:

The one randomized trial of Infliximab in patients with psoriasis showed promising results. However there were no comparative studies with standard treatment options such as phototherapy. The literature regarding the use of Infliximab to treat ulcerative colitis includes only a small number of patients.

**Methotrexate alone for patients with severe RA**

Approximately 50% of people who use Infliximab (Remicade) alone develop antibodies to the medication, which results in loss of clinical response. Methotrexate impairs this antibody response to negligible levels, so that the therapeutic effect is maintained. If a patient cannot tolerate Methotrexate it seems appropriate to allow Infliximab (Remicade) alone as an off-label use. This would be an acceptable benefit for those that do not develop the antibodies.

**PRICING:**

None

**REFERENCES:**

- The New England Journal of Medicine, A short Term Study of chimeric Monoclonal Antibody cA2 to Tumor Necrosis Factor for Crohn’s
TUMOR NECROSIS FACTOR (TNF) ALPHA INHIBITORS FOR TREATMENT OF RHEUMATOID ARTHRITIS (RA) AND OTHER CHRONIC DISEASES
RX501.051
POSTED DATE: 8/22/2003
EFFECTIVE DATE: 12/1/2003


• FDA, Department of Health and Human Services, FDA Approval Letter, Infliximab, August 24, 1998.


DISCLAIMER:

State and federal law, as well as contract language, including definitions and specific inclusions/exclusions, takes precedence over Medical Policy and must be considered first in determining coverage. The member’s contract benefits in effect on the date that services are rendered must be used. Any benefits are subject to the payment of premiums for the date on which services are rendered. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

HMO Blue Texas physicians who are contracted/affiliated with a capitated IPA/medical group must contact the IPA/medical group for information regarding HMO claims/reimbursement information and other general polices and procedures.